Clinical and laboratory manifestations of elderly onset psoriatic arthritis: a comparison with younger onset disease

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Abstract

***Objective*—Although the influence of age on clinical and laboratory features has been widely demonstrated in many arthropathies, studies on elderly onset (> 60 years) psoriatic arthritis (EOPsA) are rare. This study compares manifestations at onset and two year outcome of EOPsA with those of younger onset PsA (YOPsA).**

***Patients and methods*—Sixty six consecutive PsA patients with disease duration < 1 year, 16 EOPsA (>60 years) and 50 YOPsA (≤60 years) were admitted to a prospective study. Clinical, laboratory, and radiographic assessment were carried out at admission and after two years. HLA class I and bone scintigraphy were also recorded. In 10 patients with EOPsA and 24 with YOPsA it was possible to obtain synovial fluid, which was subsequently analysed for local inflammatory indices, including interleukin (IL) 1β, IL6, and IL8.**

***Results*—Presenting manifestations of EOPsA differed from YOPsA in number of active joints (mean (SD)) (12.2 (6.3) *v* 6.7 (4.6), p<0.001), foot bone erosions (2.7 (1.2) *v* 1.1 (1.1), p<0.001), erythrocyte sedimentation rate (64.2 (35.3) *v* 30.5 (30.0) mm 1st h, p<0.001), C reactive protein (3.9 (2.0) *v* 1.3 (1.3) mg/dl, p<0.001) and synovial fluid IL1β (8.0 (4.7) *v* 3.0 (3.0) pg/ml, p<0.001) and IL6 (828.2 (492.6) *v* 469.3 (201.4) pg/ml, p<0.005). No differences were found in the number of subjects with dactylitis, pitting oedema, HLA-B27, or signs of sacroiliac and sternoclavicular joint involvement at bone scintigraphy. After two years, progression was more evident in EOPsA than in YOPsA, as the number of new erosions in the hands and also the C reactive protein were higher in EOPsA patients.**

***Conclusion*—PsA has a more severe onset and a more destructive outcome in elderly people (onset >60 years) than in younger subjects. This behaviour may be influenced by immune changes associated with aging, as suggested by the higher concentrations of IL1β and IL6 found in the synovial fluid of EOPsA than in YOPsA.**

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The influence of age on occurrence, course, and outcome of rheumatic diseases has been frequently outlined. Classic examples are polymyalgia rheumatica, characteristically found in aging, and rheumatoid arthritis (RA), which may have different clinical and laboratory features according to the age of presentation.[1 2]

Psoriatic arthritis (PsA) has been only marginally considered in the elderly, probably because of the assumption that this disease, like the entire group of seronegative spondyloarthritis (SNSPA), rarely begins later in life.[3] Furthermore, although late onset SNSPA described in recently published papers[4–8] does report some cases of PsA, conclusions concerning the influence of age on PsA are difficult to interpret because of differences in the age groups examined by the various authors.

In this study, we prospectively evaluated presenting manifestations and two year outcome of elderly onset PsA (EOPsA) in comparison with younger onset PsA (YOPsA), to ascertain whether in PsA too, as in other rheumatic diseases, age influences the type of disease.

Methods

Sixty six consecutive patients with PsA (Moll and Wright criteria),[9] 16 EOPsA (> 60 years) and 50 YOPsA (<60 years), with disease duration < 1 year, attending our Division of Rheumatology, Institute of Internal Medicine, University of Padova, were admitted to the study. All patients had psoriasis and those with rheumatoid factor were excluded from the study. The disease duration was calculated from the onset of symptoms.

Clinical, laboratory, and radiographic assessments were carried out at admission and after two years, while HLA-B27 and bone scintigraphy were assessed only at the first examination. Clinical assessment included number of active joints (joint line tenderness and/or stress pain and/or effusion) and the presence of dactylitis or pitting oedema. The radiographs were read by the same observer who has previously shown this method to be reproducible with less than 2% intra-observer variation. The films were blinded to assessor for name and date of birth before scoring.

Laboratory investigations included erythrocyte sedimentation rate (ESR), serum C reactive protein (CRP, normal values <0.6 mg/dl), and HLA typing for B27, carried out by conventional microcytoxicity assay.[10]

At the first examination, 10 patients with EOPsA and 24 with YOPsA showed knee

Table 1 Presenting features of elderly onset (EOPsA) and younger onset (YOPsA) psoriatic arthritis

Presenting features	*EOPsA (n=16)*	*YOPsA (n=50)*	*p*
Age at onset (y)	65.1 (6.7)	44.2 (11.1)	—
M/F	8/8	23/27	NS
Active joints no (mean (SD))	12.2 (6.3)	6.7 (6.6)	<0.001
Dactylitis no (%)	6 (37.5)	15 (30)	NS
Pitting oedema no (%)	3 (18.7)	4 (8)	NS
HLA-B27 no (%)	4 (25)	12 (24)	NS
Radiograph bone erosions hands no (mean (SD))	2.3 (2.1)	2.2 (2.2)	NS
Radiograph bone erosions feet no (mean (SD))	2.7 (1.2)	1.1 (1.1)	<0.001
Scintigraphic active sacroiliac joints no (%)	4 (25)	15 (30)	NS
Scintigraphic active sternoclavear joints no (%)	4 (25)	17 (34)	NS
Erythrocyte sedimentation rate (mm 1st h) (mean (SD))	64.2 (35.3)	30.5 (30.0)	<0.001
C reactive protein (mg/dl) (mean (SD))	3.9 (2.0)	1.33 (1.3)	<0.001

For significance at 0.05 level, with 12 comparisons, Bonferroni adjustment requires a p value of ⩽0.05/12=0.004.

Table 2 Synovial fluid findings in elderly onset (EOPsA) and younger onset (YOPsA) psoriatic arthritis

	EOPsA (n=10)	*YOPsA (n=24)*	*p*
Volume (ml)	62.5 (67.8)	57.8 (43.9)	NS
WBC ($\times 10^3$/mm^3)	7.3 (3.6)	12.4 (10.0)	NS
Neutrophils (%)	64.5 (22.2)	56.2 (13.1)	NS
IL1β (pg/ml)	8.0 (4.7)	3.0 (3.0)	<0.001
IL6 (pg/ml)	828.2 (492.6)	469.3 (201.4)	<0.005
IL8 (pg/ml)	417.0 (386.4)	307.0 (382.8)	NS

WBC = white blood cells; IL = interleukin. For significance at 0.05 level, with six comparisons, Bonferroni adjustment requires a p value of ⩽0.05/6=0.008. Data shown as mean (SD).

Table 3 Treatment of elderly onset (EOPsA) and younger onset (YOPsA) psoriatic arthritis at two years

Treatment	*EOPsA, (n) (%) (n=16)*	*YOPsA, (n) (%) (n=50)*	*p*
Second line drugs	15 (93.7)	42 (84)	NS
Hydroxychloroquine	5 (31.2)	10 (20)	NS
Gold salts	2 (12.5)	5 (10)	NS
Sulphasalazine	2 (12.5)	15 (30)	NS
Methotrexate	6 (37.5)	10 (20)	NS
Cyclosporin	0	2 (4)	NS
Prednisone >5 mg/day	7 (43.7)	5 (10)	NS
Mg/prednisone/day	7.3 (2.2)	2.3 (1.8)	<0.001

For significance at 0.05 level, with six comparisons, Bonferroni adjustment requires a p value of ⩽0.05/8=0.006. Data shown as mean (SD).

synovial effusions, so that arthrocenthesis could be performed and subsequently synovial fluid (SF) analysed. Two ml of SF were collected into lithium heparin for white blood cell (WBC) count. The remaining SF was centrifuged at 3000 rpm for 10 minutes and the supernatant was stored at −20°C in multiple small volumes. Interleukin (IL) 1β, IL6, and IL8 were determined using a commercially available sensitive and specific enzyme linked immunoabsorbent assay (ELISA), (IL1β: R and D Systems, USA, limit of detection 0.3 pg/ml; IL6: Bender Med Systems, Austria; limit of detection 4 pg/ml; IL8: R and D Systems, USA, limit of detection 3 pg/ml).

Table 4 Outcome at two years of elderly onset (EOPsA) and younger onset (YOPsA) psoriatic arthritis

Outcome features	*EOPsA (n=16)*	*YOPsA (n=50)*	*p*
Active joints no	8.1 (4.2)	4.7 (3.6)	NS
Radiograph bone erosions hands no	4.4 (3.0)	2.7 (2.0)	NS
Radiograph bone erosions feet no	4.7 (2.2)	2.1 (1.2)	<0.001
Erythrocyte sedimentation rate (mm 1st h)	38.4 (15.2)	26.3 (15.0)	NS
C reactive protein (mg/dl)	2.2 (1.0)	0.9 (0.9)	<0.001

*For significance at 0.05 level, with six comparisons, Bonferroni adjustment requires a p value of ⩽0.05/5=0.001. Data shown as mean (SD).

For statistical analysis, Student's *t* test and χ^2 were used for differences. As multiple comparisons were performed, p values for type 1 errors are given for each reported difference; Bonferroni adjustment was applied to maintain an overall significance level of 0.05. Data are shown as mean (SD).

Results

PRESENTING FEATURES

The age at disease onset of 16 patients with EOPsA was 65.1 (6.7) years (range 61–73) and that of 50 patients with YOPsA was 44.2 (11.1) years (range 21–59). Eight of the 16 patients with EOPsA and 23 with YOPsA were men. The distribution of joint findings in the older group using Wright and Moll classification was polyarticular in seven, oligoarticular in six, and spondylitis in two. No patients with arthritis mutilans or with classic PsA, in which distal interphalangeal joints are predominantly involved, were found. As shown in table 1, disease onset was more severe in EOPsA than in YOPsA, as demonstrated by the higher number of active joints (12.2 (6.3) *v* 6.7 (6.6), p<0.001), foot bone erosions (2.7 (1.2) *v* 1.1 (1.1), p<0.001), ESR (64.2 (35.3) *v* 30.5 (30.0) mm 1st h, p<0.001), and CRP (3.9 (2.0) *v* 1.3 (1.3) mg/dl, p<0.001). No differences were observed for other indices. In addition (table 2), the SF concentrations of IL1β (8.0 (4.7) pg/ml *v* 3.0 (3.0) pg/ml, p<0.001), and IL6 (828.2 (492.6) pg/ml *v* 469.3 (201.4) pg/ml, p<0.005), but not those of IL8 were also higher in EOPsA than in YOPsA.

TWO YEAR OUTCOME

Two years later (table 3), almost all (15 of 16=93.7%) EOPsA and 42 of 50 (84%) YOPsA patients had been treated with slow acting anti-rheumatic drugs (SAARDs). The percentage of patients treated with SAARDs did not differ between the two groups, although hydroxychloroquine and methotrexate were more frequently used in EOPsA than in YOPsA (31.2% *v* 20% and 37.5% *v* 20%, respectively) and sulphasalazine in YOPsA than in EOPsA (30% *v* 12.5%). In addition, the mean dose (mg) of prednisolone/day was higher in EOPsA (7.3 (2.2)) than in YOPsA (2.3 (1.8), p<0.001).

After two years (table 4), both progression and activity were more evident in EOPsA subjects compared with YOPsA. The number of new erosions in the foot significantly progressed for both groups while the number of erosions in the hand progressed only in EOPsA (p=0.023). In these patients the number of foot bone erosions (4.7 (2.2) *v* 2.1 (1.2), p<0.001) and the serum concentrations of CRP (2.2 (1.0) *v* 0.9 (0.9), p <0.001) were also higher than in YOPsA. It is also noteworthy that other features (number of active joints, number of radiographic erosions, and ESR) were more severe in EOPsA than in YOPsA at two years, although the difference was not significant.

Discussion

Our study indicates that both onset manifestations and outcome of PsA in elderly patients are more severe than in younger subjects.

To compare EOPsA with YOPsA, we used the same age criterion of 60 commonly applied to the study of RA in the elderly (EORA).[2] To our knowledge, this is the first study comparing these age groups in PsA. Furthermore, there are very few studies that define age limits, usually 50 or 55 years, for late onset PsA or SNSPA, probably because of the assumption that SNSPA rarely occurs in aging.[3] However, Kaipiainen-Seppänen recently reported that in 1990 the annual incidence rate of PsA in Finland was 7.7 in 55–64, 3.6 in 65–75, and 3.1 in 75–84 year olds, respectively.[11]

Furthermore, 17 of 65 (26.1%) were aged over 55 years. The prevalence of elderly onset in the 66 consecutive patients with PsA (24.2%) of our study was quite similar to that reported by Kaipiainen-Seppänen.[11]

Among features we observed at onset, several differences were found between EOPsA and YOPsA. EOPsA showed a greater number of clinically active joints and radiographic bone erosions in the foot than YOPsA. For the detection of sacroilitis we used the bone scintigraphy. Although it is useful to specify that this method may have some limitations in the diagnosis of sacroilitis, no difference was observed between the two groups. EOPsA showed higher values of laboratory indices of inflammation, such as ESR and CRP, and higher SF concentrations of proinflammatory IL1 and IL6 than YOPsA.

The more severe onset found in EOPsA is similar to that observed in EORA[2] and in late onset patients with SNSPA.[8] The reasons for this difference are not easy to explain. In relation to the abrupt onset, it is possible that this reflects a more acute phase response, which is in turn mainly stimulated by proinflammatory cytokines and in particular by tumour necrosis factor (TNF), IL1, and IL6.[12 13] In keeping with this hypothesis are the SF concentrations of IL1β and IL6, higher in EOPsA compared with YOPsA. This is also in agreement with one of our previous studies concerning SF concentrations of cytokines in EORA.[14] The values of IL1β are usually lower in the SF of PsA than in RA with the exception of the polyarticular PsA variety.[15] The high levels of cytokines in elderly patients probably account for the poor response to non-steroid anti-inflammatory drugs reported in late onset SNSPA[8] and for the higher daily doses of corticosteroids required by our EOPsA patients.

In our study the disease outcome was also more severe in the elderly. This outcome differs from that of EORA, which, after an acute onset, shows a more favourable outcome than in younger subjects.[2] As suggested for the onset, it is possible that the evolution may also be influenced by a dysregulation in the production of cytokines involved in the stimulation of acute phase response, mainly IL6, TNF, and IL1β.[16] In keeping with this hypothesis, ESR and CRP were found to be higher in older than in younger normal subjects and increased with age.[17] Likewise, IL6 also increases with age,[13 16] probably because of dysregulation of IL6 gene expression in older people.[18] As found in this and other previous studies, IL6 is the most abundant cytokine in inflamed joints, particularly in RA.[14 19] However, in EORA, only IL6 was higher in comparison with younger subjects, while no differences were observed for IL1 and IL8,[14] thus suggesting that, in these patients, IL6 may act as a protective cytokine, for example, by increasing the values of metalloproteinase inhibitors and inhibiting the production of TNFα.[20]

The different pattern of cytokines found in the two diseases may at least partly explain the worse outcome of EOPsA in comparison with that of EORA. Moreover, we have seen that in the SF of EOPsA IL1β was also increased, indicating that the more erosive evolution of EOPsA in comparison with YOPsA is related to the high values of this proinflammatory cytokine, strongly involved in joint destruction.[21] In EOPsA, IL6 may not be sufficient to counterbalance the effects of IL1β and may perhaps act synergically.[22]

In conclusion, this study demonstrates that in PsA, as in other rheumatic diseases, initial clinical features and outcome in the elderly differ from those of younger patients. Thus, EOPsA may represent a clinical subset mainly characterised by a more acute onset and more severe outcome, requiring adequate and rapid therapeutic intervention.

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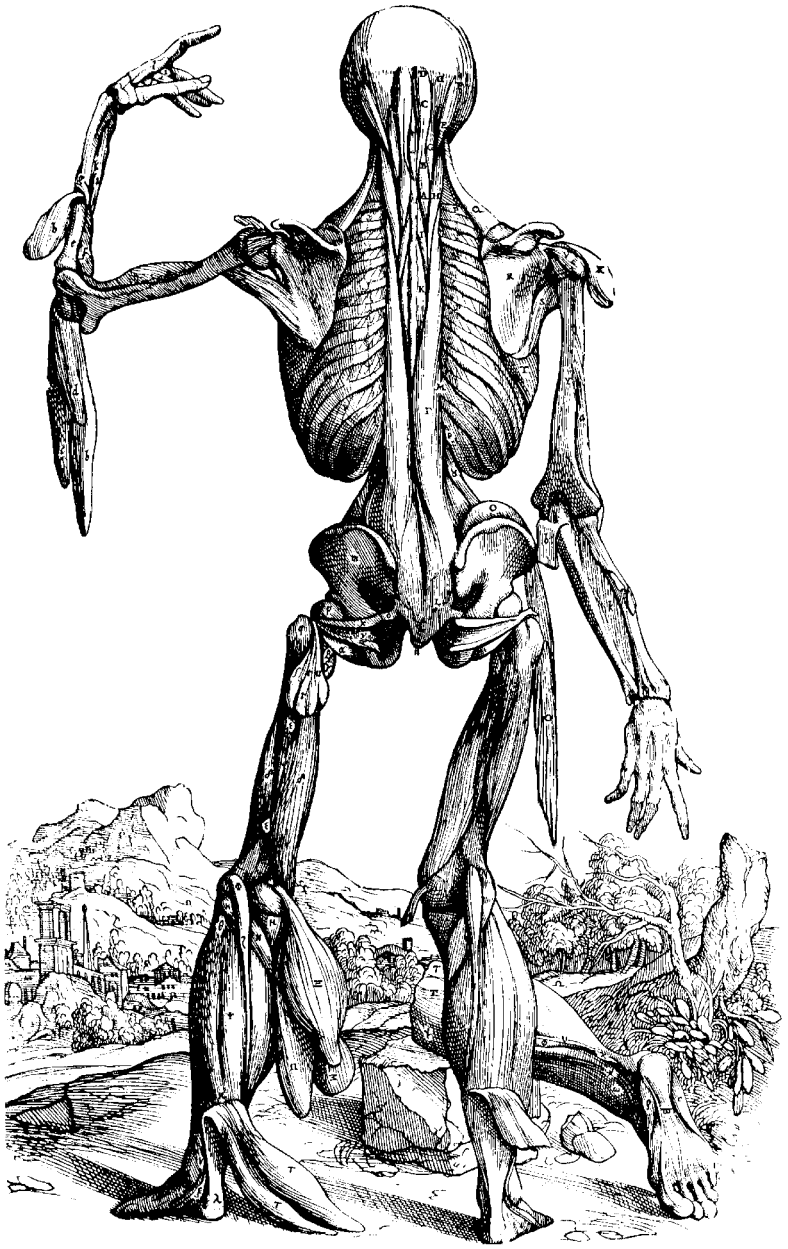

Vesalius 1543: The thirteenth plate of the muscles.
In this, the penultimate plate of the posterior series, the deeper spinal muscles are exposed, but Vesalius was very confused on their arrangement. On the right, iliocostalis is seen dependent and quadratus lumborum more clearly exposed. Teres major, the three heads of triceps hanging from the olecranon, brachialis, pronator teres and supinator seen hanging, are the muscles illustrated. In the gluteal region, apart from the other short lateral rotators of the hip, obturator externus is demonstrated with internus turned down on the left. In the thigh, the adductor mass has been turned down on the left, exposing vastus lateralis and medialis. In the leg, reflection or excision of the gastrocnemius displays the deeper muscles, plantaris, popliteus and soleus. The superficial dissection of the sole of the foot reveals the plantar fascia.